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(54) Title: RESERVOIR FOR PREPARING DIALYSATES

(57) Abstract

The present invention relates to a reservoir for storage and supply of a soluble powder material for use in a haemodialysis, haemofiltration or haemodiafiltration procedure, the reservoir having a fluid inlet means adapted to be releasably connected to a fluid supply line and a fluid outlet means adapted to be releasably connected to a fluid discharge line via which a dialysis solution comprising a solution of the soluble powder material in a fluid supplied in the fluid supply line is supplied to a dialysis apparatus during a haemodialysis, haemofiltration or haemodiafiltration procedure; characterised in that the reservoir has at least one openable and securely reclosable access port through which, when open, the soluble powder material may be supplied to or removed from the reservoir.

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RESERVOIR FOR PREPARING DIALYSATES

The present invention relates to a reusable reservoir for use in a haemodialysis, haemofiltration or haemodiafiltration procedure.

Haemodialysis is a method of cleansing the blood of patients whose kidney function is impaired. In haemodialysis procedures, the patient's blood is supplied to one side of a permeable membrane located in a dialysis apparatus. Dialysis membranes are usually formed from polyacrylonitrile or polysulphone. To the other side of the membrane is supplied a dialysis fluid containing an electrolyte solution. In a dialysis procedure, the patient's blood is pumped against the membrane, maintaining a controlled low positive blood-to-dialysate pressure gradient. By reverse osmosis waste products in the blood diffuse through the membrane into the dialysis fluid.

Haemodiaflilration and haemofiltration procedures also take advantage of permeable filter membranes to remove blood waste products. In both procedures, a more permeable filter is used than in haemodialysis and the consequent blood fluid loss is greater than in haemodialysis. Normally, this fluid must be replaced at least in part, for example by one of the methods described above. Haemodialysis, haemodiafiltration and haemofiltration procedures all require the use of an electrolyte-containing fluid either as a dialysis fluid or as a fluid replacement fluid, or both. Historically, different electrolyte mixtures have been used, the choice being influenced by a large number of technical considerations such as the type of apparatus available, the effects of any given electrolyte and also the chemical stability of certain electrolyte-containing solutions. For example, when artificial kidney machines were first used in the 1950's and 1960's, dialysis fluid containing as its principal component sodium bicarbonate was prepared in large batches prior to use in a number of treatment sessions. Sodium bicarbonate was a natural choice because of its inherent buffering capacity. However, technical difficulties were encountered especially with regard to unwanted precipitation of calcium and magnesium carbonates in the pre-formed batches. To prevent this unwanted precipitation, it was necessary to bubble carbon dioxide gas through the solution continuously, a costly and inconvenient procedure.

During the 1960's sodium acetate was used in preference to sodium

bicarbonate. Sodium acetate was perceived to have a number of advantages over sodium bicarbonate. These included an absence of problems with precipitation of insoluble salts in the dialysis solution. Sodium acetate was also perceived to have advantageous metabolic properties in that acetate is easily metabolised by the patient's liver.

A major advantage of using sodium acetate was that it became possible to prepare dialysis liquids from single liquid concentrates. Typically, one part of such a concentrate would be diluted 35 times with water before being used in a dialysis procedure. This simple preparative procedure is not available when using bicarbonate buffers because of the immediate precipitation of insoluble carbonates when all the necessary salts, including bicarbonate, are mixed together in one concentrate. The use of sodium acetate as a buffer meant that dialysis liquid could be prepared simply and conveniently at the patient's bedside.

During the 1970's however, it emerged that, whilst sodium acetate had many preparative advantages over sodium bicarbonate, it had, at least in some patients, undesirable side effects. In particular, it was demonstrated that acetate in dialysis fluid was linked with vascular instability and arterial hypotension in certain patients. When large surface dialysers were used, too much acetate was transferred into the blood and patients suffered a number of undesirable symptoms. It became clear that, for all its preparative disadvantages, sodium bicarbonate was much the better dialysis buffer, in medical terms, than sodium acetate.

The preferred use of sodium bicarbonate as a dialysis buffer combined with the attendant stability problems of that material in pre-use liquid concentrate form has led to a growth in dialysis systems which utilise cartridges of powdered solid sodium bicarbonate. Such cartridges are manufactured as sealed units containing sufficient sodium bicarbonate for a single dialysis procedure. The cartridge is attached to a dialysis apparatus comprising a water supply line. A portion of water flowing in the supply line is diverted through the cartridge and subsequently reunited with the original water stream under carefully controlled conditions to provide a final fluid for supply to the dialysis membrane, the fluid having a pre-determined quantity of sodium bicarbonate dissolved therein. Similar systems have also been used generally in the field of drug delivery. Thus, for example, WO-A-86/03416 teaches

a drug delivery apparatus preventing local and systemic toxicity which enables the passive delivery of a drug to the intravenous system of a patient. The apparatus of WO-A-86/03416 comprises a chamber for receiving a beneficial agent such as a drug. the chamber having a fluid pathway therethrough for effecting a regulated supply of the beneficial agent intravenously to a patient.

One commercial system currently in use is described in EP-A-0278100. This discloses a system for preparing a fluid for a medical procedure by mixing of at least one concentrate in powder form with water. The system contains a cartridge containing a soluble powder material. When used as a dialysis system water is supplied by a first fluid conducting means to the dialysis membrane. An adjustable portion of the fluid thus supplied is diverted through the powder-containing cartridge. If the powder is sodium bicarbonate then the dialysis may be effected using a solution of sodium bicarbonate at a controlled concentration, which solution results after recombination under controlled conditions of the diverted and undiverted portions of the water in the fluid conducting means.

The system of EP-A-0278100 and other conventional commercial systems suffer from a number of disadvantages, including the constant need of the user to replace cartridges after a single use thereof.

According to the present invention there is provided a reservoir for storage and supply of a soluble powder material for use in a haemodialysis, haemofiltration or haemodiafiltration procedure, the reservoir having a fluid inlet means adapted to be releasably connected to a fluid supply line and a fluid outlet means adapted to be releasably connected to a fluid discharge line via which a dialysis solution comprising a solution of the soluble powder material in a fluid supplied in the fluid supply line is supplied to a dialysis apparatus during a haemodialysis, haemofiltration or haemodiafiltration procedure; characterised in that the reservoir has at least one openable and securely reclosable access port through which, when open, the soluble powder material may be supplied to or removed from the reservoir.

The provision of an openable and securely reclosable access port provides significant advantages over conventional disposable cartridges used in dialysis procedures. The purchase of disposable cartridges represents a significant financial cost in the running of dialysis units and cost savings will be made by any unit

choosing to switch to the reusable reservoir of the invention. Conventional cartridges are wasteful of their powder contents because they generally contain more powder than is necessary for one procedure. This is particularly the case when a patient requires only a short dialysis because a full cartridge must nevertheless be used and cannot be re-used because of the danger of infection.

In one preferred embodiment of the invention. the reservoir comprises a first inner chamber and an outer chamber, the first inner chamber comprising a first orifice communicating with the fluid inlet means and a second orifice communicating with the outer chamber of the reservoir. The purpose of the inner chamber is to ensure even distribution of the inlet fluid over the inlet end of the outer chamber containing the dialysis powder. This has the advantage of conserving powder by ensuring as much wetting as possible of the powder contained in the outer chamber.

Even more preferably, a plurality of second orifices are provided in the first inner chamber. This embodiment of the invention is designed to enhance the even distribution of inlet fluid over the powder by providing a "sprinkling" action.

The first inner chamber of the reservoir may be a longitudinal chamber communicating with the fluid inlet means and protruding inwardly into the outer chamber of the reservoir. In this case and when a plurality of second orifices are provided. the first inner chamber may be closed at its inwardly protruding end but have a number of lateral second orifices. Substantially any number of second orifices may be employed in a cartridge according to the invention. Preferably, at least three up to about 12 or more, even more preferably four second orifices are employed. In one preferred embodiment, four second orifices are employed and are located symmetrically around the first inner chamber. The first inner chamber may be of substantially any shape. for example of hexagonal or rectangular cross section. although often a cylindrical shape will be used for ease of construction. In its simplest aspect. the purpose of the first inner chamber and second orifice or orifices is to enable a fluid supplied to the reservoir via the fluid inlet means to be distributed over the surface of any soluble powder material contained within the outer chamber of the reservoir when the reservoir is in use. The use of a plurality of second orifices tends to improve the even distribution of fluid over the inlet end of the reservoir.

There is no limitation either on the number of second orifices or their location or on the shape and/or size of the first inner chamber provided that the first inner chamber serves the purpose for which it was designed, which is to direct fluid supplied from the fluid inlet means onto a powder located in the outer chamber. One advantage of the sprinkling function of the first inner chamber is that channelling of fluid through the powder in the outer chamber of the reservoir is substantially avoided. The avoidance of channelling improves the reliability of the reservoir. Another advantage of the first inner chamber of a reservoir according to the present invention is that the smoothness of flow of fluid through the reservoir when in use is less susceptible than conventional cartridges to slight changes in pressure of the fluid supplied via the fluid inlet means.

In one embodiment of the invention, the reservoir comprises a second inner chamber comprising a first orifice communicating with the fluid outlet means and a second orifice communicating with the outer chamber of the reservoir.

In another preferred embodiment of the invention, the fluid inlet means comprises a nipple protruding from the reservoir to which nipple a fluid supply line may be connected. Conveniently, the fluid outlet means also comprises a protruding nipple to which a fluid outlet line may be connected. The shape and/or size of such nipples may be chosen to fit a range of commercially available dialysis machines.

An openable port is required in the reservoir for supplying or removing a soluble powder material such as sodium bicarbonate therethrough. Conveniently and for ease of construction and maintenance, it is preferred that the reservoir be openable in the region of a fluid inlet end and/or in the region of a fluid outlet end. In one preferred embodiment the reservoir is openable both in the region of its fluid inlet end and in the region of its fluid outlet end. Conveniently, in one embodiment, the reservoir is constructed of a hollow tube which is threaded at both its fluid inlet end and its fluid outlet end. In this case, two threaded caps, a fluid inlet cap and a fluid outlet cap, are provided. The fluid inlet cap attaches to the fluid inlet end of the reservoir and the fluid outlet cap attaches to the fluid outlet end of the reservoir. The fluid inlet cap in this case is provided on its inner face with the first inner chamber of the reservoir and on its outer face with the fluid inlet means. The fluid outlet cap is provided on its outer face with the fluid outlet means. Conveniently, both caps are

fitted with a resilient 'O' ring, for example of natural or synthetic rubber, to ensure sealing efficiency against the hollow tube. In addition, the fluid outlet cap may be fitted with a filtration device to prevent egress of undissolved powder material from the reservoir when in use.

The fluid outlet end of the reservoir is conveniently constructed with a stepped portion which may be arranged to be seated in a cartridge cradle in a range of commercially available dialysis units. In some cases, it may be necessary to provide an adaptor between the reservoir and the commercial dialysis machine. Accordingly, the invention further provides an adaptor for use with a reservoir of the invention comprising a plug portion for insertion into the corresponding socket of a dialysis machine, the plug portion having two openings and means, optionally in combination with the socket, for ensuring non-communication between said openings, the adaptor further comprising means for supplying via the first of said two openings a fluid for supply to the reservoir and means for recovering via the second of said two openings a solution of powder from the reservoir for use in a dialysis procedure.

In one preferred embodiment of the invention, the reservoir is tapered towards its fluid outlet end. Such tapering ensures smoother flow of the fluid through the powder. In one embodiment, the tapering is achieved by means of a tapered sleeve which may be inserted in a close fit arrangement with the reservoir.

In order that the invention may be clearly understood and fully carried into effect, an embodiment thereof will now be more particularly described with reference to the accompanying drawings, in which:

Figure 1 is a vertical cross-section of a reservoir designed in accordance with a first embodiment of the present invention;

Figure 2 is a vertical cross-section of a reservoir designed in accordance with a second embodiment of the invention;

Figure 3 is a cross-section through an adaptor for use with the reservoir of Figure 2: and

Figure 4 is a plan view from above of the adaptor of Figure 3.

Referring to Figure 1, there is shown a reservoir (1) for the storage and supply of a soluble powder material such as sodium bicarbonate (not shown) for use in a

haemodialysis, haemofiltration or haemodiafiltration procedure.

The reservoir (1) comprises an outer chamber (2) which is a hollow cylindrical acrylic tube manufactured by an injection moulding process. Outer chamber (2) has screw-threaded portions (3) at its upper and lower ends respectively. At the upper end of reservoir (1) is shown removable cap (4) which is secured to chamber (2) by means of screw-threaded portions (5) on cap (4). Fluid tight engagement of cap (4) and chamber (2) is assisted by a resilient 'O' ring (6) of natural or synthetic rubber. Cap (4) is injection moulded from polycarbonate and has a central orifice (7). Orifice (7) communicates at its upper end with fluid inlet nipple (8) and at its lower end with first inner chamber (9). First inner chamber (9) is provided with four orifices (10) evenly spaced around the circumference of first inner chamber (9).

Nipple (8) is shaped to be securable to a fluid inlet line from a commercially available dialysis machine such as the Gambro AK-10 system or the COBE C2RX system.

At the lower end of the chamber (2) can be seen bottom cap (11) secured to chamber (2) by a screw-threaded portion generally indicated by reference numeral (12). Fluid tight engagement of cap (11) and chamber (2) is assisted by a resilient 'O' ring (13) of natural or synthetic rubber. Cap (11) is conveniently injection moulded from polycarbonate. Cap (11) has an instepped portion (14) in which sits a filter (15). The purpose of filter (15) is to prevent small particles of undissolved material escaping from reservoir (1) when the reservoir is in use. Any convenient filter material such as a nylon mesh may be used. Conveniently, the mesh size is from about 25 micrometers to about 50 micrometers.

Cap (11) is formed integrally with nipple (16) which is shaped to receive a fluid outlet line from any commercial dialysis system. Cap (11) is also provided with a stepped portion (17) which may serve to seat the reservoir (1) in a corresponding cradle of a commercial dialysis system.

Seated within the lower end of chamber (2) is tapered sleeve (18) which is a moulded polycarbonate sleeve arranged to fit slidably into chamber (2) and to direct the flow of fluid through chamber (2) towards a central region of the bottom end of chamber (2).

The dimensions of a typical reservoir in accordance with the invention and suitable for use with the Gambro AK-10 system are as follows:

chamber (2) is cylindrical with an external diameter of 3.150 inches (8.001cm) and a length of 6.788 inches (17.241cm);

threaded portions (3) on chamber (2) extend 5/8 inches (1.588cm) from each end of chamber (2);

fluid inlet cap (4) and fluid outlet cap (11) each have an external diameter of 4 inches (10.16cm) and an internal diameter (circumferenced by screw threaded portions (5) and (12) respectively) of 3.360 inches (8.534cm);

nipples (8) and (16) are slightly chamfered at their respective protruding ends; each protrudes from a respective external face of cap (4) or cap (11) by 9/16 inches (1.429cm) and each has an external diameter of 3/8 inches (0.953cm) at its respective protruding end, not including any chamfered portion of the end;

stepped portion 17 on fluid outlet cap (11) has a diameter of 2.1 inches (5.33cm) and a depth of 0.5 inches (1.27cm);

the total longitudinal distance between respective ends of nipples (8) and (16) when the reservoir is assembled is 9.1 inches (23.1cm).

In use, the reservoir is partially filled with a quantity of sodium bicarbonate, optionally in conjunction with other materials, useful in dialysis. Typically, the reservoir is charged with a mass of 500g sodium bicarbonate in readiness for a single dialysis treatment. The reservoir is then connected at its fluid inlet end and at its fluid outlet end to a suitable dialysis apparatus such as the Gambro AK-10 or the COBE C2RX and a dialysis treatment is carried out in accordance with methods which are well known to those skilled in the art.

Thus, in a dialysis procedure using a cartridge according to the invention, the cartridge is connected to apparatus comprising a first fluid conducting means having a first end for communicating with a source of water to withdraw water into the first fluid conducting means and a second end for delivering a prepared solution; second fluid conducting means having a first end for communicating with a source of water and a second end communicating with the fluid inlet end of the reservoir for introducing water into the reservoir to produce a concentrate fluid containing dissolved powder concentrate in water: third fluid conducting means communicating

with the outlet end of the reservoir and with a mixing point in the first fluid conducting means intermediate said first and second ends for conducting the concentrate fluid from the reservoir into the first fluid conducting means to be mixed with fluid being conducted through the first fluid conducting means thereby to produce a prepared solution in the first fluid conducting means for delivery to the second end of the first fluid conducting means.

Conveniently, the apparatus will comprise measuring means in the first fluid conducting means downstream of the mixing point for measuring the composition of the prepared solution obtained by the mixing of the concentrate fluid and water in the first fluid conducting means. The apparatus may further comprise flow regulating means in the third fluid conducting means responsive to said measuring means for controlling the flow of the concentrate fluid from the reservoir.

When a dialysis treatment utilising a reservoir according to the invention has been completed, the reservoir may be detached from the dialysis apparatus and, after appropriate sterilising treatment, may be charged once again with sodium bicarbonate in readiness for a further dialysis treatment. Sterilisation of the reservoir in between treatments may be effected by any of a number of methods which are well known to those skilled in the art. One convenient method of sterilisation is to rinse excess sodium bicarbonate from the reservoir with water before soaking the resevoir in a solution of sodium dichlorisocyanurate (Sanichlor™) at a suitable concentration.

Referring to Figure 2, there is shown a reservoir (101) which is suitable for use with the commercially available Fresenius 4008E dialysis machine. Reservoir (101) comprises comprises an outer chamber (102) which is a hollow cylindrical acrylic tube manufactured by an injection moulding process. Outer chamber (102) has a screw-threaded portion (103) at its upper end. At the upper end of reservoir (101) is shown removable cap (104) which is secured to chamber (102) by means of screw-threaded portions (105) on cap (104). Fluid tight engagement of cap (104) and chamber (102) is assisted by a resilient 'O' ring (106) of natural or synthetic rubber. Cap (104) is injection moulded from polycarbonate and has two orifices (107 and 107a). Orifice (107) communicates at its upper end with fluid inlet nipple (108) and at its lower end with first inner chamber (109). First inner chamber (109)

is provided with a single orifice (110) at one end of first inner chamber (109).

Second inner chamber (111) communicates at its lower end with outer chamber 102 and at its upper end with fluid outlet nipple (112).

In use of reservoir (101), the reservoir is filled with a suitable quantity of sodium chloride and lines are taken from each of fluid inlet nipple (108) and fluid outlet nipple (112) for connection to an adaptor suitable for use with the Fresenius machine referred to above. The adaptor is shown in Figures 3 and 4 and comprises a plug portion (113) for insertion into the corresponding socket (not shown) of a Fresenius machine and a receiving portion (114) for receiving lines from the fluid inlet nipple (108) and the fluid outlet nipple (112). Plug portion (113) comprises three concentric cylindrical walls (115, 116 and 117) of polyethylene standing up from a base portion (118). Standing down from base portion (118) is a chamber (119) which communicates via orifice (120) with the fluid supply line of the dialysis machine (not shown) and via orifice (121) with a line (not shown) taken from fluid inlet nipple (108). The chamber (119) is traversed by a conduit (122) which has an opening (123) at its upper end communicating with the fluid intake line of the dialysis machine (not shown) and an opening (124) at its lower end communicating with a line (not shown) taken from fluid outlet nipple (112) of reservoir (101).

Fluid is supplied to a powder, such as sodium bicarbonate, contained in outer chamber (102) and a solution of the powder is drawn into second inner chamber (111) via filter (125) by the action of a pump in the dialysis machine (not shown).

As with the reservoir of Figure 1, at the end of a dialysis procedure, reservoir (101) may simply be detached from the dialysis machine and prepared for re-use. Thus, the reservoir (101) is opened by removing cap (104), excess powder is rinsed from the reservoir and the reservoir is sterilised by a suitable procedure prior to recharging with powder for further use.

CLAIMS:

1. A reservoir for storage and supply of a soluble powder material for use in a haemodialysis, haemofiltration or haemodiafiltration procedure, the reservoir having a fluid inlet means adapted to be releasably connected to a fluid supply line and a fluid outlet means adapted to be releasably connected to a fluid discharge line via which a dialysis solution comprising a solution of the soluble powder material in a fluid supplied in the fluid supply line is supplied to a dialysis apparatus during a haemodialysis, haemofiltration or haemodiafiltration procedure; characterised in that the reservoir has at least one openable and securely reclosable access port through which, when open, the soluble powder material may be supplied to or removed from the reservoir.

2. A reservoir according to claim 1, characterised in that the reservoir comprises a first inner chamber and an outer chamber, the first inner chamber comprising a first orifice communicating with the fluid inlet means and a second orifice communicating with the outer chamber of the reservoir.

3. A reservoir according to claim 2, characterised in that a plurality of second orifices are provided in the first inner chamber.

4. A reservoir according to claim 3, characterised in that the first inner chamber of the reservoir is a longitudinal chamber communicating with the fluid inlet means and protruding inwardly into the outer chamber of the reservoir, said first inner chamber being closed at its protruding end but having a number of second orifices in its side.

5. A reservoir according to claim 3 or claim 4, characterised in that the first inner chamber of the reservoir comprises at least three second orifices.

6. A reservoir according to any one of claims 3 to 5. characterised in that the first inner chamber of the reservoir comprises between three and twelve second orifices.

7. A reservoir according to any one of claims 3 to 6, characterised in that the first inner chamber of the reservoir comprises four second orifices.

8. A reservoir according to any one of claims 3 to 7, characterised in that the second orifices of the first inner chamber of the reservoir are arranged symmetrically around the first inner chamber.

9. A reservoir according to any one of claims 1 to 8, characterised in that the reservoir comprises a second inner chamber comprising a first orifice communicating with the fluid outlet means and a second orifice communicating with the outer chamber of the reservoir.

10. A reservoir according any one of claims 1 to 9, characterised in that the fluid inlet means comprises a nipple upstanding from the reservoir

11. A reservoir according to any one of claims 1 to 10, characterised in that the fluid outlet means comprises a nipple protruding from the reservoir

12. A reservoir according to any one of claims 1 to 11, characterised in that the reservoir includes in the region of its fluid outlet means a filtration device to prevent egress of undissolved powder material from the reservoir when in use.

13. A reservoir according to any one of claims 1 to 12, characterised in that an exterior face of the reservoir adjacent fluid outlet means therefore comprises a stepped portion adapted to be seated in a cartridge cradle of a dialysis apparatus.

14. A reservoir according to any one of claims 1 to 13, characterised in that it includes an interior tapered portion tapering towards the fluid outlet means of the

reservoir.

15. An adaptor for use with a reservoir according to any one of claims 1 to 14, comprising a plug portion for insertion into the corresponding socket of a dialysis machine, the plug portion having two openings and means, optionally in combination with the socket, for ensuring non-communication between said openings, the adaptor further comprising means for supplying via the first of said two openings a fluid for supply to the reservoir and means for recovering via the second of said two openings a solution of powder from the reservoir for use in a dialysis procedure.

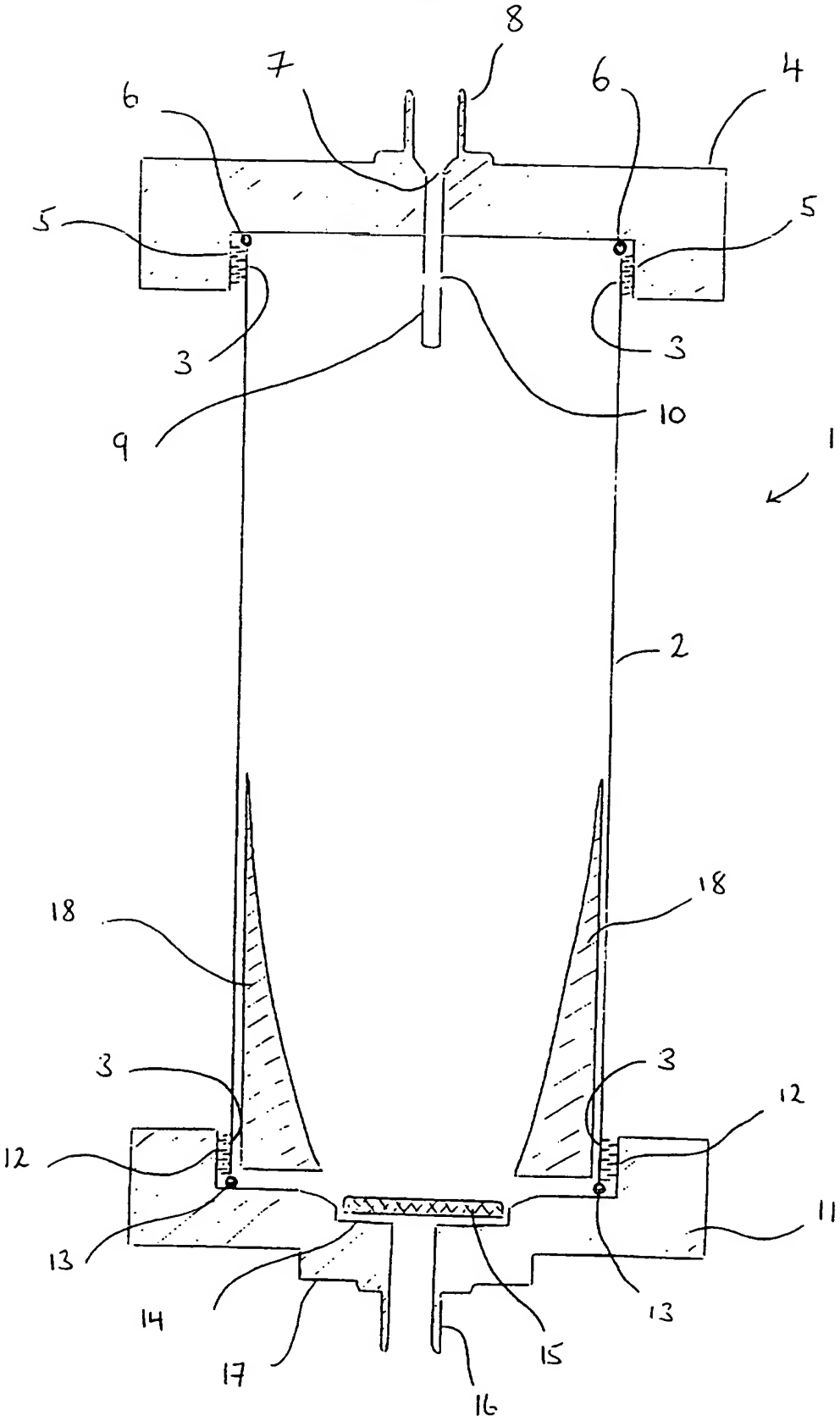

FIG. 1

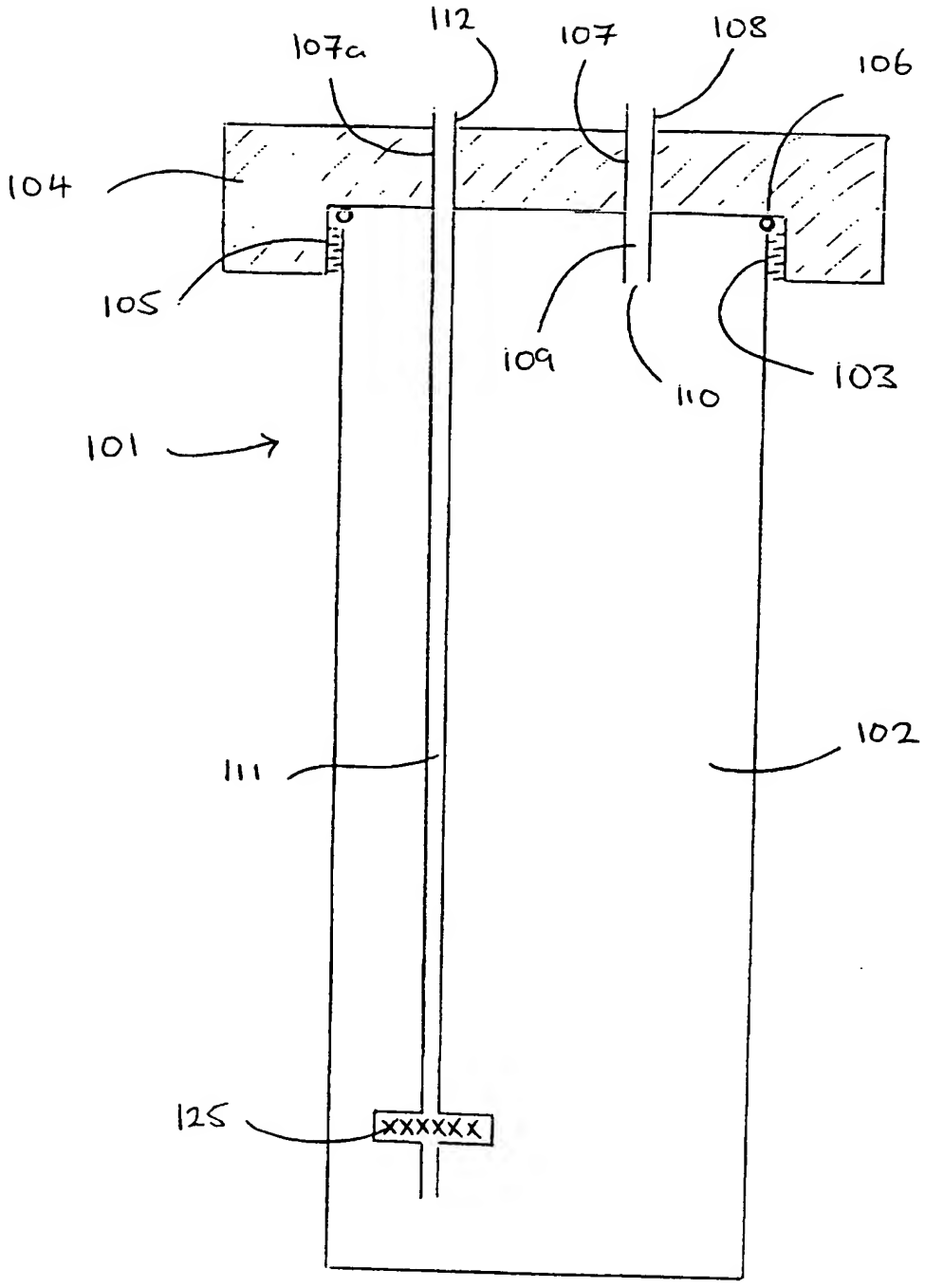

FIG. 2

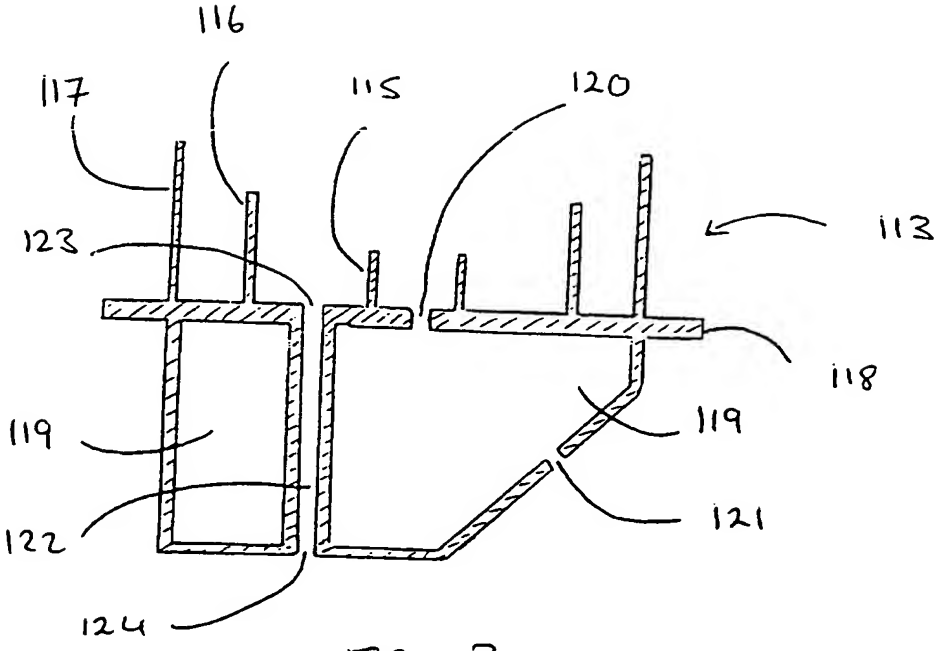
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FIG. 3

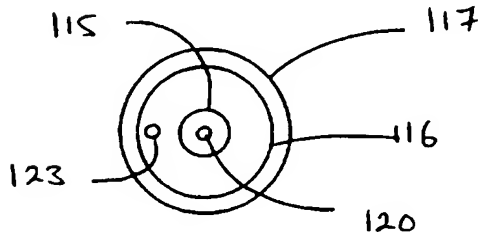
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FIG. 4

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/GB 97/00460

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M1/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 536 645 A (SAUERESSIG) 14 April 1993 see column 6, line 14 - column 8, line 11 see column 10, line 6 - line 20 see figures 1-5,8	1,2, 10-12,14
X	DE 91 11 524 U (ZAUNBAUER) 5 December 1991 see page 5, line 5 - page 6, line 19 see figure 1	1,10-12, 14
X	FR 2 569 560 A (GRANGE) 7 March 1986 see page 2, line 22 - page 5, line 17 see figure 2	1-6,8,12

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
18 June 1997	27.06.97

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inter mal Application No
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